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Original research

Standardization of morbidity assessment in breast cancer surgery using the Clavien Dindo Classification

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ABSTRACT

Introduction: There are no published data on standardized scoring systems for morbidity after breast cancer surgery. Aim of the study was to establish the Clavien Dindo Classification (CDC) as assessment tool and to identify risk factors for morbidity after breast surgery investigating new techniques including oncoplastic surgery and neoadjuvant chemotherapy.
Patients and methods: Between 2008 and 2010, data were retrospectively evaluated from 485 women with breast cancer who underwent surgery at a university hospital. The CDC was used to assess the severity of postoperative complications. Multivariable analyses were adjusted by body-mass index, smoking, diabetes mellitus and tumour size.
Results: Overall complications (CDC 1–4) were reported in 28.7%. Second surgery related to major complications (CDC 3–4) was mandatory in 4.7%. Axillary dissection was an independent predictor for CDC 1–4 in all patients ($P = 0.008$, OR of 1.81, 95%CI 1.17–2.82). We found no independent predictor for CDC 3–4. Oncoplastic surgery increased the rate of wound infections ($P = 0.010$, OR: 2.94, 95%CI 1.30–6.67) and necroses ($P < 0.001$, OR: 8.38, 95%CI 3.28–21.4). Axillary dissection elevated wound infection ($P = 0.040$, OR: 2.07, 95%CI 1.03–4.14) and seroma rates ($P < 0.001$, OR: 2.46, 95%CI 1.51–4.01). Neoadjuvant chemotherapy had no impact on morbidity.
Conclusion: The CDC is a valid assessment tool for future clinical trials and may be useful for hospital quality control. While axillary dissection and oncoplastic surgery raised morbidity, no single factor predicted for morbidity related second surgery.
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1. Introduction

Accreditation of Breast Health Centers [1] and implementation of multidisciplinary Health Boards [2] are assessment processes. Health care management uses them to define standards and improve professional performance of hospitals for two major aims: efficient patient safety and cost control. They provide data concerning quality indicators as well as objective treatment evaluation [3]. Standardization and resource economics are mandatory for optimal cooperation of hospital management and government systems to assure high quality services to patients. The rate of postoperative morbidity indicates quality of surgery in Breast Health Centers. Furthermore, major complications significantly raise median hospital costs [4].

Morbidity after breast surgery is low [5,6]. Novel therapies such as neoadjuvant chemotherapy and immediate techniques of oncoplastic surgery have increasingly been used. However, little is known about the effect of such new techniques on postoperative morbidity [7–9]. Moreover, standardized morbidity-measurement tools are still lacking.

In this respect, the Clavien Dindo Classification (CDC) is a validated and simple classification of surgical complications used for general and oncologic surgery [10]. It classifies the extent of postoperative morbidity in correlation to the therapy management. Low-Grade morbidities undergo conservative treatment, high-Grade complications are re-operated or treated at the Intensive Care Unit. Postoperative mortality is scored with the highest Grade of the CDC. In summary, the Clavien Dindo Classification is therapy-oriented and may be easily adopted for oncologic breast surgery.

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Table 1
Clavien Dindo Classification: morbidity in patients with breast cancer.

Grade	Description of complication treatment in general	Breast morbidity
Grade 1	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics and electrolytes and physiotherapy. This Grade also includes wound infections opened at the bedside.	Abscess: 1 Bleeding: 2 Necrosis: 6 (+seroma: +2; +lymphedema: +1) Seroma: 62 Wound infection: 1
Grade 2	Requiring pharmacological treatment with drugs other than such allowed for Grade 1 complications. Blood transfusions and total parenteral nutrition are also included.	Abscess: 5 (+seroma: +1) Bleeding: 6 Necrosis: 5 Seroma: 6 Wound infection: 8 (+seroma: +17; +lymphedema: +1) Lung embolism: 1
Grade 3	3a: intervention not under general anaesthesia 3b: intervention under general anaesthesia	Abscess: 3 (+seroma: +1; +necrosis: +3) Bleeding: 15 Necrosis + seroma: 1 Wound infection: 7 (+seroma: +1; +necrosis: +2)
Grade 4	Life-threatening complication (including complications of the Central Nervous System) requiring Intermediate Care/ Intensive Care Unit management 4a: single-organ dysfunction (including dialysis) 4b: multiorgan dysfunction	Perforation of the stomach: 1
Grade 5	Death of a patient	Hospital mortality: 0

The aim of the study was to investigate the usefulness of the CDC as tool to measure postoperative morbidity in breast cancer surgery. Oncoplastic surgery and neoadjuvant chemotherapy as well as other surgical parameters were assessed regarding their relation to postoperative morbidity after adjusting for known risk factors such as smoking [6], diabetes mellitus (DM) [6], overweight (BMI $>$ 35) [5,6,11] and tumour size [8,12].

2. Patients and methods

2.1. Study design

We retrospectively evaluated patients with primary breast cancer after breast surgery and pathologically confirmed R0 resection (not touching the ink) who were treated at the Division of General Surgery, Medical University of Vienna, between January 2008 and December 2010. Data were taken from the hospital database. After each visit at the outpatient ward, our study nurse prospectively processed data into a pre-existing computer worksheet. Data were then transferred into an Excel spreadsheet for further statistical analyses. Patient characteristics, pathological reports, treatment and follow up data have been continuously recorded. Data were retrospectively examined and updated by the end of 2011 with the patient information system of the Medical University of Vienna comprising all data from patients who were treated at the institution. The study has been approved by the local Ethic Authorities (EK Nr 051/2011). The study was conducted according to the criteria of Good Clinical Practice and the Declaration of Helsinki of 1964, updated in Seoul 2008. All patients subsequently underwent radiotherapy in the case of breast conserving surgery followed by chemo- and/or endocrine therapy based on interdisciplinary tumour board decisions. Neoadjuvant chemotherapy was given to patients if mastectomy was primarily indicated or in cases of HER-2/neu positivity or triple negativity with tumours larger than 2 cm in diameter.

2.2. Neoadjuvant chemotherapy

Most patients received neoadjuvant chemotherapy within prospective randomized trials conducted by the Austrian Breast and Colorectal Cancer Study Group (ABCSG-14 and ABCSG-24) [13,14]. ABCSG-14 compared three cycles of epirubicin 75 mg/m^2 and docetaxel 75 mg/m^2 (ED; on day 1, every three weeks, plus granulocyte colony-stimulating factor on days 3–10 of each cycle) to six cycles of the same regimen as neoadjuvant treatment for breast cancer [13]. Based upon a proposed synergistic effect of docetaxel and capecitabine, ABCSG-24 compared three cycles of ED plus capecitabine (EDC; epirubicin 75 mg/m^2 and docetaxel 75 mg/m^2 on day 1, capecitabine 1000 mg/m^2 BID days 1–14, every three weeks, plus pegfilgrastim 6 mg on day 2 of each cycle) with standard six cycles of ED as established in ABCSG-14. Patients with HER-2/neu-positive disease were additionally randomized to neoadjuvant trastuzumab every three weeks or control [14].

2.3. Surgical procedure

Indications for mastectomy included progressive carcinoma after neoadjuvant chemotherapy, multicentricity, inflammatory breast cancer, unfavourable relation of tumour size and breast size with inability to perform breast conservation with adequate margins [15] and patients' wish. Lumpectomy with macroscopic 1 cm free margins (microscopically not touching the ink for R0) without skin excision was performed for breast conserving surgery. In case of neoadjuvant chemotherapy and clinical downstaging, surgery was performed within the new borders.

Sentinel lymph node dissection was offered to all patients with clinically non-suspicious axilla using blue dye only. Patients after neoadjuvant chemotherapy underwent axillary lymph node dissection. Level I and II lymphadenectomy was carried out in the presence of histologically verified sentinel lymph node macrometastasis or of palpatory suspicious lymph nodes. Non-palpable lesions were localized preoperatively with a hook wire. These patients received perioperative antibiotic treatment with penicillin or second-generation cephalosporin. Frozen section analyses were routinely performed during surgery to reduce the need for second surgery [16].

The combination of oncologic resection with plastic surgical techniques during one surgical step (oncoplastic surgery) was offered to some patients with a resection volume $\geq$ 25% [9]. We either used the doughnut oncoplastic or other techniques of breast

reduction [7,9]. Technical devices such as Ligasure™ or Ultracision™ were not used in this cohort.

All patients received an axillary suction drain after sentinel lymph node dissection or axillary dissection and an in-breast capillary drainage after breast conservation. Patients had 2 subcutaneous "in-breast" suction drains after mastectomy. The main factor for discharge was the day of removing the axillary and/or subcutaneous "in-breast" suction drain. Before removal, it was mandatory that the fluid volume must not exceed 50 ml/24 h. As to the in-breast capillary drainage, we used an Easy Flow™ with a capillary effect. This was drawn out on the first or second day after surgery.

2.4. Follow up

Patients were followed up on the 10th postoperative day at the surgical outpatient ward and during oncologic routine follow up care. Local morbidity was recorded in our computer database (Krankenanstalteninformationssystem = KIS). Skin necrosis, axillary or in-breast seroma formation, bleeding and infection with or without abscess were evaluated. Seroma formation was defined as clinically apparent wound fluid occurring after removal of the suction drains. In general, therapy ranged from conservative treatment with wound bandage and antibiotics up to serial seroma punctures, abscess drainage under local anaesthesia and reoperation for bleeding or large infections.

2.5. Morbidity classification

CDC assesses the severity Grade of postoperative complications from 1 to 5 (Table 1). Grade 0 means no complication, Grade 1–2 minor, 3–4 major morbidity and Grade 5 is related to postoperative death [10]. The CDC was assessed retrospectively by two independent physicians.

2.6. Statistical analyses

Categorical data were described with absolute and relative frequencies. Continuous variables were described using mean ± standard deviation in the case of approximate normal distribution and using median and interquartile range (IQR) otherwise. The inverse Kaplan–Meier method was used to calculate the median follow up time. Univariate and multivariable logistic regression were employed in order to investigate the potential effect of various established and new risk factors. Interaction terms of a cohort indicator (breast conserving surgery versus mastectomy) and each risk factor were used in each model to test for a cohort specific effect. Since none of these interaction terms was significant, all models contain only the main effect of the cohort indicator and results are reported for the total data set (breast conserving surgery and mastectomy). In the case of the primary outcome variable, postoperative morbidity (CDC 1–4), the high number of events allowed for a full multivariable analysis. In contrast, the number of events for major morbidity (CDC 3–4) as well as single complications only allowed for one adjustment variable. We chose BMI which was detected as an important predictor of postoperative morbidity in two large series [5,6]. BMI and tumour size were log-transformed as independent variables. The reported p-values were the results of two-sided tests. $P < 0.05$ was considered statistically significant. Due to the exploratory character of this part of the study, no correction was performed among the list of secondary outcomes (CDC 0–2 versus 3–4, single complications): P values and Confidence Intervals (CI) are to be interpreted accordingly. All calculations were carried out using SAS statistical software Version 9.2 (SAS Institute Inc., Cary, NC, USA 2008).

Table 2
Demographic data.

	Breast conserving therapy ($n = 357$)	Mastectomy ($n = 128$)
TNM		
pTis	21 (5.9%)	13 (10.2%)
yT0	1 (0.3%)	0
pT1/2	330 (92.4%)	88 (68.8%)
pT3/4	5 (1.4%)	27 (21.1%)
N0	245 (68.6%)	62 (48.4%)
N0 i+[a]	5 (1.4%)	1 (0.8%)
N1mic	21 (5.9%)	4 (3.1%)
N1/2/3	86 (24.1%)	61 (47.7%)
G1	72 (19.6%)	6 (4.7%)
G2	166 (46.5%)	65 (50.8%)
G3/x	119 (33.3%)	57 (44.5%)
Lymph node dissection		
Sentinel dissection[b]	3 (2–4)	3 (2–5)
Axillary dissection[b]	14 (12–19)	15 (11–18)

[a] Isolated tumour cells.
[b] Data are medians with interquartile range in parentheses.

3. Results

3.1. Demographic data

TNM-status and Grading are given in Table 2. Ninety-two patients (25.8%) in the breast conserving surgery group and 47 patients (36.7%) in the mastectomy group were premenopausal. 34 patients (9.5%) before breast conserving surgery and 28 patients (21.9%) before mastectomy underwent neoadjuvant chemotherapy. Median follow up was 11 (IQR 1–24) months after breast conserving surgery and 17 (IQR 4–30) months after mastectomy.

3.2. Surgical outcome

Primary surgical procedures and reoperations are presented in Table 3. Out of 485 surgically treated patients, sentinel lymph node dissection was done in 300 breast conserving surgery (84.0%) and 85 mastectomy (66.4%) patients. Axillary dissection was twice as high in the mastectomy group (60.2%) compared to breast conserving surgery patients (30.8%). oncoplastic surgery rates were equal in both groups (breast conserving surgery: 10.9%, mastectomy: 10.2%).

3.3. Postoperative morbidity and mortality

Overall, CDC 1–4 was higher in the mastectomy cohort compared to breast conserving surgery (Table 3). Grade 1 was reported in 75, Grade 2 in 41 and Grade 3 in 22 patients. Grade 4 was related to one breast conserving surgery patient due to a non-breast surgery-related complication (Fig. 1). Seroma rates were twice as high in the mastectomy group compared to breast conserving surgery. Two patients, one in each cohort, suffered from a chronic lymph oedema after axillary dissection at one-year follow up. Detailed morbidity data after axillary dissection, oncoplastic surgery and neoadjuvant chemotherapy are presented in Table 3.

Second surgery was mandatory in 106 patients (21.9%). Major postoperative complications (CDC 3–4) were treated surgically in 5 mastectomy and 18 breast conserving surgery patients (Fig. 1). 50 patients (10.3%) were reoperated due to inadequate tumour excision. Re-excision was reported in one patient (1/128: 0.8%) after primary mastectomy and in 29 breast conserving surgery patients (29/357: 8.1%). 20 patients (20/485: 4.1%) had to undergo mastectomy after prior breast conserving surgery due to residual disease. Isolated axillary dissection as second surgery was performed in 10

Table 3
Morbidity data.

	Patients	Axillary dissection		Oncoplastic surgery		Neoadjuvant chemotherapy	
	($n = 485$)	Yes	No	Yes	No	Yes	No
Breast conservation	$n = 357$	$n = 110$	$n = 247$	$n = 39$	$n = 318$	$n = 34$	$n = 323$
Overall morbidity (CDC[a] 1–4)	88 (24.6%)	40 (36.4%)	48 (19.4%)	12 (30.8%)	76 (23.9%)	8 (23.5%)	80 (24.8%)
Seroma	52 (14.6%)	28 (25.5%)	24 (9.7%)	5 (12.8%)	47 (14.8%)	6 (17.6%)	46 (14.2%)
Wound infection	28 (7.8%)	14 (12.7%)	14 (5.7%)	6 (15.4%)	22 (6.9%)	3 (8.8%)	25 (7.7%)
Necrosis	10 (2.8%)	6 (5.5%)	4 (1.6%)	4 (10.3%)	6 (1.9%)	0	10 (3.1%)
Bleeding	14 (3.9%)	5 (4.6%)	9 (3.6%)	2 (5.1%)	12 (3.8%)	0	14 (4.3%)
Abscess	13 (3.6%)	4 (3.6%)	9 (3.6%)	2 (5.1%)	11 (3.5%)	1 (2.9%)	12 (3.7%)
Mastectomy	$n = 128$	$n = 77$	$n = 51$	$n = 13$	$n = 115$	$n = 28$	$n = 100$
Overall morbidity (CDC[a] 1–4)	51 (39.8%)	33 (42.9%)	18 (35.3%)	8 (61.5%)	43 (37.4%)	13 (46.4%)	38 (38.0%)
Seroma	39 (30.5%)	27 (35.1%)	12 (23.5%)	4 (30.8%)	35 (30.4%)	11 (39.3%)	28 (28.0%)
Wound infection	9 (7.0%)	6 (7.8%)	3 (5.9%)	3 (23.1%)	6 (5.2%)	1 (3.6%)	8 (8.0%)
Necrosis	10 (7.8%)	5 (6.5%)	5 (9.8%)	5 (38.5%)	5 (4.3%)	1 (3.6%)	9 (9.0%)
Bleeding	5 (3.9%)	3 (3.9%)	2 (3.9%)	1 (7.7%)	4 (3.5%)	1 (3.6%)	4 (4.0%)
Abscess	1 (0.8%)	0	1 (2.0%)	1 (7.7%)	0	0	1 (1.0%)

[a] Clavien Dindo Classification.

patients (2.1%) due to false negative sentinel nodes. 23 patients (4.7%) underwent reoperation of the breast in combination with axillary dissection after false negative sentinel lymph node dissection dissection. There was no case of postoperative in-hospital mortality (CDC 5).

3.4. Risk factors for postoperative morbidity

In the univariate analysis, axillary dissection ($P = 0.001$, OR: 1.99), tumour size ($P = 0.021$, OR: 1.26 for each doubling of tumour size) and BMI ($P = 0.001$, OR: 3.58 for each doubling of BMI) predicted for postoperative morbidity (CDC 1–4). In the multivariable model, the effects of axillary dissection, oncoplastic surgery and neoadjuvant chemotherapy were adjusted for each other and for known risk factors. Axillary dissection was the only risk factor to show a clinically relevant and statistically significant effect on CDC 1–4 (Table 4). Furthermore, axillary dissection was a predictor of wound infections and seroma rates. Oncoplastic surgery predicted increased wound infection and necrosis rates (Table 4). All necroses were limited to the cutaneous and subcutaneous layer, no flap necroses were reported. The effect of each risk factor on the considered complications can be quantified by an odds ratio for the total set of patients (i.e. breast conserving surgery and mastectomy), since the effects were not significantly modified by distinguishing between the two cohorts (breast conserving surgery versus mastectomy).

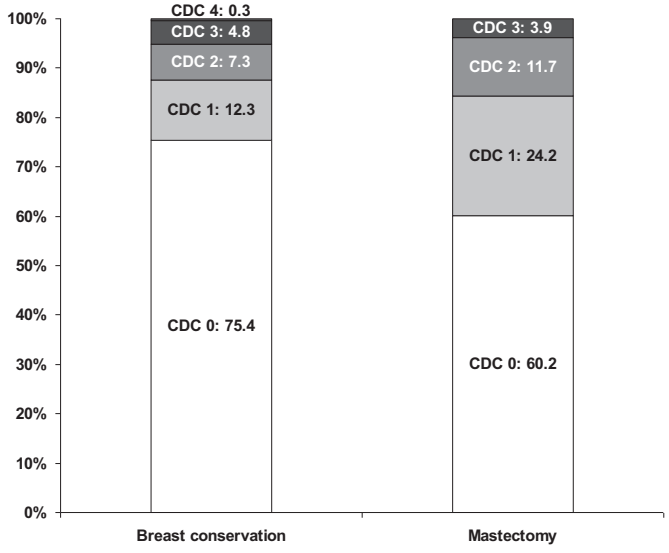

Fig. 1. Clavien Dindo Classification (CDC) grading (0 = no complication; 5 = postoperative mortality) in patients undergoing breast conserving surgery ($n = 357$) and mastectomy ($n = 128$). Data are presented as percentages.

4. Discussion

This is the first published report about using a modified CDC score to evaluate postoperative morbidity in breast cancer patients. After adjusting for known risk factors (obesity, diabetes mellitus, smoking and tumour size) our analyses demonstrated that axillary dissection was the only independent risk factor for the development of postoperative morbidity (CDC 1–4), especially related to seroma formation. Necrosis was increased after oncoplastic surgery. Both axillary dissection and oncoplastic surgery were associated with elevated wound infection rates. Other factors such as neoadjuvant chemotherapy failed to show a significant impact in multivariable analyses. Moreover, no potential risk factor was identified for complication related reoperations (CDC 3).

Reported morbidity rates after breast surgery range from 2% [5,6] to 35% [17]. This major discrepancy between the reported studies may be due to different assessment methods and morbidity definition. In order to standardize morbidity measurement, we incorporated the CDC for breast cancer patients. The CDC helps to compare data within different surgical departments [10]. It uses the complication treatment for classifying morbidity. Complications, especially minor ones, are frequently not precisely documented. Complication treatment, however, is documented well and based on hard facts. Furthermore, it is not influenced by subjective interpretation; therefore morbidity treatment documentation represents an objective tool for standardized scoring [10].

The Doc-Cert AG St. Gallen certification program for Breast Health Centers surveys morbidity data in only 2 (wound infection, post-radiation skin reactions) out of 34 items. According to the EUSOMA certification, requirements for accreditation include documentation of lymph oedema [18]. Standardized and sufficient evaluation of postoperative complications is lacking in those certification programs. The use of a modified CDC in breast cancer patients was practical in our study. We suggest using this classification for further studies and in the certification process for Breast Health Centers. Morbidity data of different centers, even using different certification programs, could be compared with each other as important quality measure.

Table 4
Multivariable analysis of risk factors for postoperative morbidity and morbidity related reoperations.

	Patients	Axillary dissection	*P* value	Oncoplastic surgery	*P* value	Neoadjuvant chemotherapy	*P* value
	($n = 485$)	OR [95% CI]		OR [95% CI]		OR [95% CI]	
Overall morbidity							
(CDC[a] 1–4)	139 (28.7%)	1.88 [1.18–2.98]	0.008	1.72 [0.91–3.23]	0.094	0.86 [0.45–1.64]	0.649
Reoperations							
(CDC[a] 3–4)	23 (4.7%)	0.88 [0.37–2.11]	0.775	1.88 [0.65–5.45]	0.245	0.48 [0.09–2.54]	0.387
Seroma	91 (18.8%)	2.46 [1.51–4.01]	<0.001	0.92 [0.43–1.98]	0.836	1.51 [0.79–2.88]	0.216
Wound infection	37 (7.6%)	2.07 [1.03–4.14]	0.040	2.94 [1.30–6.67]	0.010	1.07 [0.37–3.07]	0.902
Necrosis	20 (4.1%)	1.49 [0.60–3.70]	0.386	8.38 [3.28–21.40]	<0.001	0.40 [0.07–2.17]	0.287
Bleeding	19 (3.9%)	1.15 [0.44–3.04]	0.772	1.96 [0.60–6.46]	0.268	0.19 [0.01–3.15]	0.249
Abscess	14 (2.9%)	0.81 [0.27–2.48]	0.718	2.34 [0.68–8.02]	0.178	1.11 [0.20–6.11]	0.904

Odds ratio: overall morbidity is adjusted for body-mass index, smoking, diabetes mellitus and tumour size, all other risk factors are adjusted solely for body-mass index.
[a] Clavien Dindo Classification: CDC 4: one patient underwent reoperation and stayed at the intensive care unit afterwards.

Authors from the ACOSOG Z0011 trial recommended avoiding axillary dissection even if macrometastases were found within the sentinel lymph node [19]. That paradigm shift has been discussed very controversially. Our data support the notion to omit axillary dissection in respect to morbidity. Axillary dissection was the only independent risk factor for elevated morbidity due to seroma and infection rates. Elevated seroma accumulations facilitate the emergence of wound infections. Other authors confirmed higher morbidity rates after axillary dissection compared to sentinel lymph node dissection. Axillary dissection mainly leads to early complications, while delayed morbidity and second surgery rates were not increased [20].

In future, modern devices such as bipolar vessel-sealing devices (Ligasure™) may reduce seroma formation and make axillary dissection safer [21]. Reduced seroma amounts with shorter drainage periods and sufficient sanitation standards in the operation and hospital wards can minimize infection rates. Our data do not answer the question about long term morbidity and thus these data should not lead to support omitting axillary dissection in general.

Patients undergoing oncoplastic surgery have longer scars and more extensive mobilization of the breast parenchyma. The blood supply is hampered by preparation and the larger wound surface may promote morbidity which has been demonstrated in up to 25% of these patients [22,23]. In the literature, necrosis rates range between 16% and 25% [7,9,22,24] and delayed wound healing between 19% and 25% [23,25]. In our cohort, oncoplastic surgery raised wound infections and necrosis rates significantly without increasing second surgery rates. Delayed wound healing and extensive wounds may promote tissue infection. Therefore, stringent sterility in the operation theatre and standardized antibiotic prophylaxis are mandatory. Usually necrosis is seen at the edges of the breast skin flaps. This may be further reduced by careful dissection, leaving a thicker subcutaneous tissue in place. In the future, we hope that necrosis rates may be significantly reduced by applying new agents like Traditional Chinese Medicine herbal therapy [26].

Cytotoxic agents have shown to suppress immune function and wound healing in animal testing [27,28]. Shamberger et al. reported that a prolonged interval of cytostatic therapy followed by surgery significantly reduced morbidity [28]. Donker et al. compared patients with skin-sparing mastectomy and immediate prosthetic reconstruction who had undergone neoadjuvant chemotherapy versus no neoadjuvant chemotherapy [29]. Seroma rates were equal in both cohorts, whereas skin necrosis rates were significantly higher in the control group without neoadjuvant chemotherapy. That outcome might be explained by the younger age of patients undergoing neoadjuvant chemotherapy. Broadwater et al. compared similar cohorts of women undergoing mastectomy [30]. Postoperative morbidity was equal in both groups, but seroma rates were significantly decreased in the neoadjuvant chemotherapy group compared to the control patients. The authors did not give any explanation for those data. In general, several other authors investigating morbidity after breast surgery failed to find significant differences comparing patients with and without neoadjuvant chemotherapy [8,11]. In our study, neoadjuvant chemotherapy was associated neither to increased postoperative morbidity nor higher second surgery rates.

There are several biases in our study. First, the low event rates reduce the power of the multivariable analyses. Second, patients who had a prolonged hospital stay due to a longer drainage period were not included in the morbidity assessment. Those patients usually underwent neoadjuvant chemotherapy. Although there are data showing that longer drainage periods do not reduce seroma formation we still believe that the increased seroma formation after neoadjuvant chemotherapy seen in our personal praxis is thus not reflected in our trial.

In conclusion, the Clavien Dindo Classification may be recommended to document morbidity as part of certification programs for Breast Health Centers. However, this classification has to be re-evaluated within another patient cohort.

Ethical approval

Data were retrospectively examined and updated by the end of 2011 with the patient information system of the Medical University of Vienna comprising all data from patients who were treated at the institution.

The study has been approved by the local Ethic Authorities (EK Nr 051/2011).

The study was conducted according to the criteria of Good Clinical Practice and the Declaration of Helsinki of 1964, updated in Seoul 2008.

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Author contribution

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Veronika Ferenc: Data collections.
Michael Schütz: Data collections.
Andreas Gleiss: Data analysis.
Peter Dubsky: Study design.
Raimund Jakesz: Study design, data analysis.
Michael Gnant: Study design, data analysis.
Florian Fitzal: Study design, data analysis, writing.

Conflict of interest

All authors declare no conflict of interest.

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References

[1] D.P. Winchester, The National Accreditation Program for Breast Centers: quality improvement through standard setting, Surg. Oncol. Clin. N. Am. 20 (3) (2011) 581–586, http://dx.doi.org/10.1016/j.soc.2011.01.011.

[2] E.M. Kesson, G.M. Allardice, W.D. George, H.J. Burns, D.S. Morrison, Effects of multidisciplinary team working on breast cancer survival: retrospective, comparative, interventional cohort study of 13 722 women, BMJ 26 (2012) e2718, http://dx.doi.org/10.1136/bmj.e2718.

[3] S.H. Cheng, C.J. Wang, J.L. Lin, C.F. Horng, M.C. Lu, S.M. Asch, et al., Adherence to quality indicators and survival in patients with breast cancer, Med. Care 47 (2) (2009) 217–225, http://dx.doi.org/10.1097/MLR.0b013e3181893c4a.

[4] J.B. Dimick, S.L. Chen, P.A. Taheri, W.G. Henderson, S.F. Khuri, D.A. Campbell Jr., Hospital costs associated with surgical complications: a report from the private-sector National Surgical Quality Improvement Program, J. Am. Coll. Surg. 199 (4) (2004) 531–537.

[5] M.B. El-Tamer, B.M. Ward, T. Schifftner, L. Neumayer, S. Khuri, W. Henderson, Morbidity and mortality following breast cancer surgery in women: national benchmarks for standards of care, Ann. Surg. 245 (5) (2007) 665–671.

[6] C. de Blacam, A.A. Ogunleye, A.O. Momoh, S. Colakoglu, A.M. Tobias, R. Sharma, et al., High body mass index and smoking predict morbidity in breast cancer surgery: a multivariate analysis of 26,988 patients from the national surgical quality improvement program database, Ann. Surg. 255 (3) (2012) 551–555, http://dx.doi.org/10.1097/SLA.0b013e318246c294.

[7] F. Fitzal, G. Nehrer, D. Hoch, O. Riedl, S. Gutharc, M. Deutinger, et al., An oncoplastic procedure for central and medio-cranial breast cancer, Eur. J. Surg. Oncol. 33 (10) (2007) 1158–1163.

[8] W.A. Peled, K. Itakura, R.D. Foster, D. Hamolsky, J. Tanaka, C. Ewing, et al., Impact of chemotherapy on postoperative complications after mastectomy and immediate breast reconstruction, Arch. Surg. 145 (9) (2010) 880–885, http://dx.doi.org/10.1001/archsurg.2010.163.

[9] F. Fitzal, G. Nehrer, M. Deutinger, R. Jakesz, M. Gnant, Novel strategies in oncoplastic surgery for breast cancer: immediate partial reconstruction of breast defects, Eur. Surg. 39 (6) (2007) 330–339, http://dx.doi.org/10.1007/s10353-007-0373-x.

[10] D. Dindo, N. Demartines, P.A. Clavien, Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey, Ann. Surg. 240 (2) (2004) 205–213.

[11] P. Forouhi, J.M. Dixon, R.C. Leonard, U. Chetty, Prospective randomized study of surgical morbidity following primary systemic therapy for breast cancer, Br. J. Surg. 82 (1) (1995) 79–82.

[12] D. Christante, S.J. Pommier, B.S. Diggs, B.T. Samuelson, A. Truong, C. Marquez, et al., Using complications associated with postmastectomy radiation and immediate breast reconstruction to improve surgical decision making, Arch. Surg. 145 (9) (2010) 873–878, http://dx.doi.org/10.1001/archsurg.2010.170.

[13] G.G. Steger, A. Galid, M. Gnant, B. Mlineritsch, A. Lang, C. Tausch, et al., Pathologic complete response with six compared with three cycles of neoadjuvant epirubicin plus docetaxel and granulocyte colony-stimulating factor in operable breast cancer: results of ABCSG-14, J. Clin. Oncol. 25 (15) (2007) 2012–2018.

[14] G.G. Steger, R. Greil, A. Lang, M. Rudas, F. Fitzal, B. Mlineritsch, et al., Austrian Breast and Colorectal Study Group (ABCSG), Epirubicin and docetaxel with or without capecitabine as neoadjuvant treatment for early breast cancer: final results of a randomized phase III study (ABCSG-24), Ann. Oncol. 25 (2) (2014) 366–371, http://dx.doi.org/10.1093/annonc/mdt508.

[15] M. Morrow, Margins in breast-conserving therapy: have we lost sight of the big picture? Expert Rev. Anticancer Ther. 8 (8) (2008) 1193–1196, http://dx.doi.org/10.1586/14737140.8.8.1193.

[16] O. Riedl, F. Fitzal, N. Mader, P. Dubsky, M. Rudas, M. Mittlboeck, et al., Intraoperative frozen section analysis for breast-conserving therapy in 1016 patients with breast cancer, Eur. J. Surg. Oncol. 35 (3) (2009) 264–270, http://dx.doi.org/10.1016/j.ejso.2008.05.007.

[17] A.L. Vinton, L.W. Traverso, P.C. Jolly, Wound complications after modified radical mastectomy compared with tylectomy with axillary lymph node dissection, Am. J. Surg. 161 (5) (1991) 584–588.

[18] R.W. Blamey, L. Cataliotti, EUSOMA accreditation of breast units, Eur. J. Cancer 42 (10) (2006) 1331–1337.

[19] A.E. Giuliano, K.K. Hunt, K.V. Ballman, P.D. Beitsch, P.W. Whitworth, P.W. Blumencranz, et al., Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial, J. Am. Med. Assoc. 305 (6) (2011) 569–575, http://dx.doi.org/10.1001/jama.2011.90.

[20] T. Ashikaga, D.N. Krag, S.R. Land, T.B. Julian, S.J. Anderson, A.M. Brown, et al., National Surgical Adjuvant Breast, Bowel Project. Morbidity results from the NSABP B-32 trial comparing sentinel lymph node dissection versus axillary dissection, J. Surg. Oncol. 102 (2) (2010) 111–118, http://dx.doi.org/10.1002/jso.21535.

[21] T. Cortadellas, O. Córdoba, M. Espinosa-Bravo, C. Mendoza-Santin, J. Rodríguez-Fernández, A. Esgueva, et al., Electrothermal bipolar vessel sealing system in axillary dissection: a prospective randomized clinical study, Int. J. Surg. 9 (8) (2011) 636–640, http://dx.doi.org/10.1016/j.ijsu.2011.08.002.

[22] S.L. Spear, C.V. Pelletiere, A.J. Wolfe, T.N. Tsangaris, M.F. Pennanen, Experience with reduction mammaplasty combined with breast conservation therapy in the treatment of breast cancer, Plast. Reconstr. Surg. 111 (3) (2003) 1102–1109.

[23] A. Losken, E.T. Elwood, T.M. Styblo, J. Bostwick 3rd, The role of reduction mammaplasty in reconstructing partial mastectomy defects, Plast. Reconstr. Surg. 109 (3) (2002) 968–975.

[24] E. Chang, N. Johnson, B. Webber, J. Booth, D. Rahhal, D. Gannett, et al., Bilateral reduction mammoplasty in combination with lumpectomy for treatment of breast cancer in patients with macromastia, Am. J. Surg. 187 (5) (2004) 647–650.

[25] K.B. Clough, J.S. Lewis, B. Couturaud, A. Fitoussi, C. Nos, M.C. Falcou, Oncoplastic techniques allow extensive resections for breast-conserving therapy of breast carcinomas, Ann. Surg. 237 (1) (2003) 26–34.

[26] J. Chen, Q. Lv, M. Yu, X. Zhang, J. Gou, Randomized clinical trial of Chinese herbal medications to reduce wound complications after mastectomy for breast carcinoma, Br. J. Surg. 97 (12) (2010) 1798–1804, http://dx.doi.org/10.1002/bjs.7227.

[27] D.F. Devereux, L. Thibault, J. Boretos, M.F. Brennan, The quantitative and qualitative impairment of wound healing by adriamycin, Cancer 43 (3) (1979) 932–938.

[28] R.C. Shamberger, D.F. Devereux, M.F. Brennan, The effect of chemotherapeutic agents on wound healing, Int. Adv. Surg. Oncol. 4 (1981) 15–58.

[29] M. Donker, J.J. Hage, L.A. Woerdeman, E.J. Rutgers, G.S. Sonke, M.J. Vrancken Peeters, Surgical complications of skin sparing mastectomy and immediate prosthetic reconstruction after neoadjuvant chemotherapy for invasive breast cancer, Eur. J. Surg. Oncol. 38 (1) (2012) 25–30, http://dx.doi.org/10.1016/j.ejso.2011.09.005.

[30] J.R. Broadwater, M.J. Edwards, C. Kuglen, G.N. Hortobagyi, F.C. Ames, C.M. Balch, Mastectomy following preoperative chemotherapy. Strict operative criteria control operative morbidity, Ann. Surg. 213 (2) (1991) 126–129.